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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,298	06/12/2006	Gordon N. Gill	00015-041US1/2003-061-1MI	6198

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EXAMINER
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SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
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1652

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/552,298	<b>Applicant(s)</b> GILL ET AL.	
	<b>Examiner</b> SHERIDAN SWOPE	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 11-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☒ Claim(s) 5-10 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicants' Request for Continued Examination of September 21, 2009, in response to the Action of April 21, 2009 is acknowledged. It is acknowledged that Claims 1 and 2 have been amended. Claims 1-42 are pending. Claims 11-42 were previously withdrawn from further consideration as being drawn to nonelected inventions. Claims 1-10 are hereby reexamined.

#### ***Priority***

The priority date granted for the instant invention is April 1, 2004, the filing date of PCT/US04/10218, which disclosed the elected invention. It was previously noted that provisional application US 60/459,786 fails to disclose SEQ ID NO: 1 or 2.

In response, applicants argue that US 60/459,786 discloses information sufficient to demonstrate possession of the claimed invention at least as early as April 1, 2003. One of skill in the art would recognize that Applicants had possession of the claimed sequence by reference to the genomic sequence and protein fragments in combination with the functional and physical characteristics of the disclosure of the encoded polypeptides.

These arguments are not found to be persuasive for the following reasons. The skilled artisan would not assume that Applicants were in possession of SEQ ID NO: 1 or 2 because the protein fragments disclosed by the specification don't disclose the entire protein. At best, the skilled artisan could identify only portions of the genomic sequence as being part of the cDNA sequence. Nothing would provide which portions of the genomic sequence are the remaining exonic portions. Therefore, the priority date granted for the instant invention is April 1, 2004.

#### ***Claims-Objections***

Objection to Claims 5-10, for reciting non-elected sequences, is maintained.

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***Claim Rejections - 35 USC § 112-Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claim 2, lines 3, 4, and 5-6, the phrase “a sequence as set forth by SEQ ID NO: ...” renders the claim indefinite. It is unclear whether said phrase means “the sequence as set forth by SEQ ID NO: ...” or “any sequence set forth by SEQ ID NO: ...”. The latter would include fragments as small as dipeptides. The skilled artisan would not know the metes and bounds of the recited invention. Claims 7-10, as dependent from Claim 2, are indefinite for the same reason. For purposes of examination, it is assumed that “a sequence as set forth by SEQ ID NO: ...” means “the sequence as set forth by SEQ ID NO: ...”.

For Claim 2, lines 3, 4, and 5, the term “having” renders the claim indefinite. It is unclear whether said phrase means “consisting of” or “comprising”. The skilled artisan would not know the metes and bounds of the recited invention. Claims 7-10, as dependent from Claim 2, are indefinite for the same reason. For purposes of examination, it is assumed that “having” means “comprising”.

Any subsequent rejection based, on clarification of the above phrases and terms, will not be considered a new ground for rejection.

***Claim Rejections - 35 USC § 112-First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### **Enablement**

Rejection of Claims 1 and 7-10 under 35 U.S.C. 112, first paragraph/enablement, for reasons explained in the prior action, is maintained.

In support of their request that this rejection be withdrawn, Applicants provide the following arguments.

(A) By reciting percent identity with reference to a particular sequence along with a recited function there cannot be an almost infinite possibility of variants, but rather a subset that can be easily screened using routine skill as indicated by the Examiner.

(B) The Examiner then goes on to indicate that Cocks et al. and Meinnel et al. would be capable of modifying their defective sequence to arrive at Applicants' invention. The Examiner asserts that Cocks et al. and Meinnel et al. would be enabled to (i) select one of numerous (almost infinite) polypeptides sequences from Cocks et al., (ii) identify one sequence that would have a stop codon from an almost infinite number of sequences in the correct reading frame (i.e., any length of upstream sequences) and then (iii) insert upstream at one of almost an infinite number of points a starting methionine.

(C) The Examiner appears to indicate that Applicants are not entitled to adding or substituting amino acids having a defined structure and function using routine skill in the art.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: Guo et al, 2004 teaches that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a

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model, is 34% and that this number is consistent with other studies in other proteins (pg 9206, parag 4). Guo et al further show that the percentage of active mutants for multiple mutations appears to be exponentially related to this by the simple formula  $(.66)^x \times 100\%$  where x is the number of mutations introduced (Table 1). Applying this estimate to the protein recited in the instant application, 80% identity allows up to 52 mutations within the 260 amino acids of SEQ ID NO: 2 and, thus, only  $(.66)^{52} \times 100\%$  or  $4 \times 10^{-8}\%$  of random mutants having 80% identity would be active. The genus of any protein having 80% identity to a parent protein of 260 residues, as is SEQ ID NO: 2, can be described by  $(19_1 + 19_2 + 19_3 + \dots 19_{260})^{20} = 7.5 \times 10^{73}$  variants. Current techniques in the art (i.e., high throughput mutagenesis and screening techniques) would allow for finding a few active mutants within several hundred thousand or up to about a million inactive mutants (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish). But finding a few mutants within several billion or more, as in the claims to 80% identity to SEQ ID NO: 2, would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

(B) Reply: This is the same argument Applicants presented in their response of August 21, 2008. Applicants are directed to the reasons this argument is not found to be persuasive in the action of November 24, 2008, page 7.

(C) Reply: Applicants are entitled to have their invention encompass adding or substituting amino acids to a protein having a defined structure and function using routine skills

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in the art. However, as explained above and in the prior actions, while enablement is not precluded by the necessity for routine experimentation, if a large amount of experimentation is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification.

For these reasons and those explained in the prior actions, rejection of Claims 1 and 7-10 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 1 and 5-10 under 35 U.S.C. 102(b), as being anticipated by Venter et al, 2002 for the reasons explained in the prior action, is maintained. In support of their request that this rejection be withdrawn, Applicants provide the following arguments. Venter et al does not teach or suggest that their polynucleotide encodes a protein having a recited activity. This is the same argument Applicants provided in their prior responses. See the Action of November 24, 2008 as to why this argument is not persuasive.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection of Claims 1 and 3-10 under 35 U.S.C. 103(a) as being unpatentable over Cocks et al, 2003 in view of Meinnel et al, 1993, for the reasons explained in the prior actions, is maintained. Claim 2 is herein rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al, 2003 in view of Meinnel et al, 1993, for the same reasons.

In support of their request that this rejection be withdrawn, Applicants provide the following arguments.

(A) The Cocks et al. patent is a listing of putative sequences that may or may not have activity, that may or may not have start codons, and may or may not have stop codons. The Cocks patent is not enabling. SEQ ID NO:843, which is relied upon for the present rejection is a sequence of nearly 2000 basepairs of which only half appear to align. Applicants submit that there is no teaching or suggestion in Cocks et al. that identify a sequence set forth by Applicants having the biological activity as set forth in the claims.

(B) In order to overcome the deficiencies of Cocks et al., the Office Action combines Meinnel et al. for the teaching that nearly all proteins begin with an N- terminal Methionine. Furthermore, Meinnel et al. indicates that "most" have such a methionine, clearly some do not.

(C) As stated above, the Cocks et al. disclosure is a non-enabling disclosure for at least two reasons. First, a sequence lacking a functional utility lacks enablement (see, e.g., *In re Fisher* (Fed. Cir. 2005)). Second, the Examiner attributes enablement only to the extent that a proper start codon is inserted in any number of infinitely possible positions upstream of the sequence identified in Cocks et al. For Cocks et al. and Meinnel et al. to be enabling would require modification of their defective sequence to arrive at Applicants' invention.



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(D) Meinnel et al. is a general reference that does little to overcome the lack of enablement or description by Cocks et al. Rather, Meinnel et al. teach only that start codon's are important but does not provide any indication to one of skill in the art a reasonable expectation of any success in generating Applicants' claimed invention based upon the disclosure of Cocks et al.

(A) Reply: This argument is essentially the same as the argument Applicants provided in their prior responses. See the Action of November 24, 2008 as to why this argument is not persuasive. In addition it is noted that, for the polynucleotide of Cocks, residues 1-780 are an open reading frame with no stop codons, while residues 781-783 are a stop codon. Thus, the skilled artisan would know that residues 1-780 encode a protein having the activities inherent to its structure.

(B) Reply: If the polynucleotide of Cocks began with a methionine codon, this would be a rejection under 35 USC 102, not 35 USC 103(a).

(C) Reply: This is the same argument Applicants provided in their response of August 21, 2008. Applicants are directed to the reasons this argument is not found to be persuasive in the action of April 21, 2009, page 6.

(D) Reply: This is the same argument Applicants provided in their response of August 21, 2008. Applicants are directed to the reasons this argument is not found to be persuasive in the action of April 21, 2009, page 7.

For these reasons and those explained in the prior action, Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al, 2003 in view of Meinnel et al, 1993.

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***Allowable Subject Matter***

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

**Final Comments**

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

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It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943.

The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/  
Primary Examiner, Art Unit 1652